Truong, T.
10/088852

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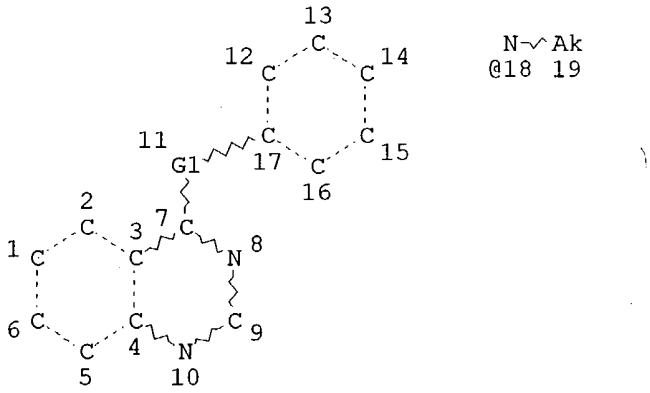
L1 STR



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GGCAT IS LOC AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
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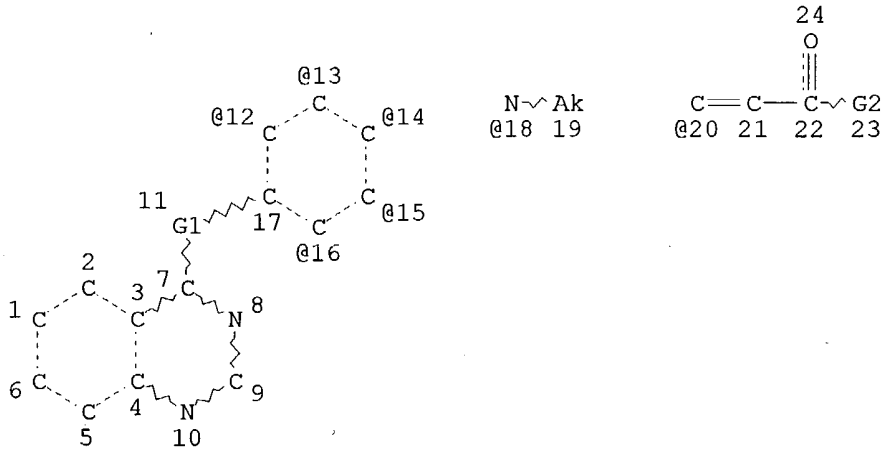
L14 STR



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DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 19

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 868 ITERATIONS 74 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 11:40:39 ON 09 NOV 2004
L16 4 S L15

E1 THROUGH E73 ASSIGNED

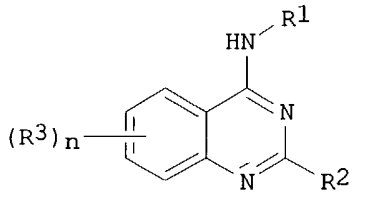
L16 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 Feb 2004
ACCESSION NUMBER: 2004:120821 CAPLUS
DOCUMENT NUMBER: 140:163886
TITLE: Preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases
INVENTOR(S): Gazit, Aviv; Levitzki, Alexander
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013091	A2	20040212	WO 2003-IL632	20030731
WO 2004013091	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-399736P P 20020801
OTHER SOURCE(S): MARPAT 140:163886
GI



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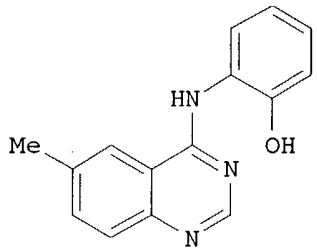


II

AB Title compds. I [R1 = (un)substituted Ph, naphthyl, etc.; R2 = H, halo, phenylamino, etc.; R3 = H, alkoxy, NO2, etc.; n = 1-3] are prepared For instance, 4-chloro-6-methylquinazoline is reacted with 2-aminophenol (EtOH, reflux, 1 h) to give II. I are potent inhibitors of protein tyrosine (PTK) kinase activity, particularly epidermal growth factor receptor (EGFR) kinase activity. I are useful in treating a variety of PTK related disorders such as cell proliferative disorders, fibrotic disorders, metabolic disorders and cancer.

IT **655248-61-6P**, 3-[2-Bromo-4-((6,7-dimethoxyquinazoline-4-yl)amino)phenyl]-2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]acrylamide **655248-62-7P**, N-Benzyl-3-[2-bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyanoacrylamide **655248-63-8P**, 3-[2-Bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyano-N-(4-phenylbutyl)acrylamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

L16 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Mar 2001
ACCESSION NUMBER: 2001:228866 CAPLUS
DOCUMENT NUMBER: 134:266317
TITLE: Preparation of quinazolines as aurora 2 kinase inhibitors
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John; Jung, Frederic Henri; Brewster, Andrew George
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021596	A1	20010329	WO 2000-GB3580	20000918

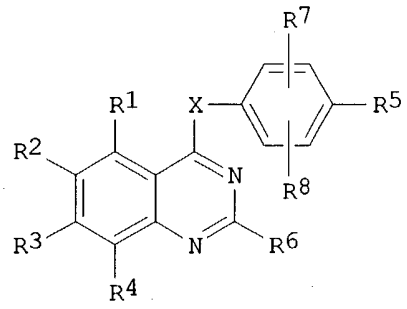
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000014116	A	20020521	BR 2000-14116		20000918
EP 1218354	A1	20020703	EP 2000-960840		20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003509499	T2	20030311	JP 2001-524975		20000918
EE 200200119	A	20030415	EE 2002-119		20000918
BG 106492	A	20030131	BG 2002-106492		20020307
ZA 2002002234	A	20030619	ZA 2002-2234		20020319
NO 2002001399	A	20020430	NO 2002-1399		20020320
PRIORITY APPLN. INFO.:			GB 1999-22154	A	19990921
			GB 1999-22170	A	19990921
			WO 2000-GB3580	W	20000918

OTHER SOURCE(S): MARPAT 134:266317

GI



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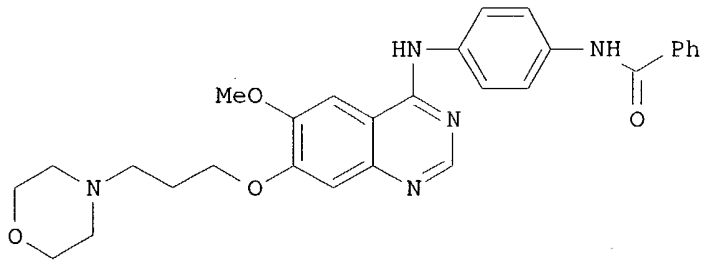

II

AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR12; R12 = H or alkyl; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R13, or R15X1; R13 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, CO2, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R15 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; R5 = NHCO2R9, NHCOR9, NHSO2R9, COR9, CO2R9, SOR9, SO2OR9, CONR10R11, SONR10R11, or SO2NR10R11; R9-R11 = independently H or (un)substituted hydrocarbyl or heterocyclyl; or R10 and R11 together with the N to which they are

attached = (un)substituted heterocyclyl; R6 = H or (un)substituted hydrocarbyl or heterocyclyl; R7 and R8 = independently H, halo, alkyl, (di)alkoxy(methyl), alkanoyl, CF3, CN, NHY2, alkenyl, alkynyl, or (un)substituted Ph, PhCH2, or heterocyclyl; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, a 7-step sequence involving (1) alkylation of morpholine with 1-bromo-3-chloropropane (49%), (2) addition of Et vanillate to yield Et 3-methoxy-4-(3-morpholinopropoxy)benzoate (100%), (3) nitration (86%), (4) reduction to the amine using 10% Pd/C (100%), (5) cycloaddn. with formamide to form the quinazoline(68%), (6) chlorination to give 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline (60%), and (7) amination with N-benzoyl-4-aminoaniline (58%) yielded II. The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.0193 μM. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.06 μM and reduced BrdU incorporation into cellular DNA by 50% at 0.159-0.209 μM.

IT **331776-88-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 4-substituted quinazoline aurora 2 kinase inhibitors for treatment of cancer and other proliferative diseases)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Mar 2001
ACCESSION NUMBER: 2001:228865 CAPLUS
DOCUMENT NUMBER: 134:266316
TITLE: Preparation of quinazoline derivatives, method of preparation and use in inhibiting aurora 2 kinase
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021595	A1	20010329	WO 2000-GB3562	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000014136	A	20020521	BR 2000-14136	20000918
EP 1218357	A1	20020703	EP 2000-962682	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003509498	T2	20030311	JP 2001-524974	20000918
EE 200200148	A	20030415	EE 2002-148	20000918
ZA 2002001831	A	20030605	ZA 2002-1831	20020305
NO 2002001395	A	20020515	NO 2002-1395	20020320
BG 106535	A	20021229	BG 2002-106535	20020320

PRIORITY APPLN. INFO.: GB 1999-22173 A 19990921
WO 2000-GB3562 W 20000918

OTHER SOURCE(S): MARPAT 134:266316
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB I or a salt, ester, amide or prodrug thereof, a method for the preparation of I and the use of the claimed compds. for inhibiting aurora 2 kinase are claimed. These compds. are useful in the treatment of cancer. In I: X is O, or S, S(O) or S(O)2 or NR10 where R10 is H or C1-6 alkyl. R5 is OR11, NR12R13 or SR11 where R11, R12 and R13 are independently optionally substituted hydrocarbyl or optionally substituted heterocyclic groups, and R12 and R13 may addnl. form together with the N atom to which they are attached, an optionally substituted aromatic or nonarom. heterocyclic ring which may contain further heteroatoms. R6 and R7 are independently H or hydrocarbyl. R8 and R9 are independently H, halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkoxymethyl, di(C1-4alkoxy)methyl, C1-4 alkanoyl, trifluoromethyl, cyano, amino, C2-5 alkenyl, C2-5 alkynyl, a Ph group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or nonarom. and may be saturated (linked via a ring C or N atom) or unsatd. (linked via a ring C atom), and which Ph, benzyl or heterocyclic group may bear on one or more ring C atoms up to 5 substituents selected from hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C2-4 alkanoyl, C1-4 alkanoylamino, C1-4 alkoxycarbonyl, C1-4 alkylthio, C1-4 alkylsulfinyl, C1-4 alkylsulfonyl, carbamoyl, N-C1-4alkylcarbamoyl, N,N-di(C1-4alkyl)carbamoyl, aminosulfonyl, N-C1-4alkylaminosulfonyl, N,N-di(C1-4alkyl)aminosulfonyl, C1-4 alkylsulfonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C1-4alkoxycarbonyl. R1, R2, R3, R4 are independently halo, cyano, nitro, C1-3 alkylthio, -N(OH)R14 (R14 is H, or C1-3 alkyl), or R16X1- (X1 represents a direct bond, -O-, -CH2-, -OC(O)-, -C(O)-, -S-, -SO-, -SO2-, -NR17C(O)-, -C(O)NR18-, -SO2NR19-, -NR20SO2- or -NR21- (R17, R18, R19, R20 and R21 each independently represents H, C1-3 alkyl or C1-3alkoxyC2-3alkyl), and R16 is H, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy). A method for preparing I comprises reacting II where X, R8 and R9 are as defined above, R1', R2', R3', R4' are groups R1, R2, R3, R4 as defined above resp., or precursors thereof; and R85 is a leaving group, with HCR6:CR7C(O)R5', where R6 and R7 are as defined above, R5' is a group R5 as defined above or a precursor group therefore; and thereafter if

desired or necessary, converting any precursor groups R1', R2', R3', R4' or R5' to groups R1, R2, R3, R4 or R5 resp., or changing a group R5 to a different such group. The compds. of the invention inhibit the serine/threonine kinase activity of the aurora 2 kinase and thus inhibit the cell cycle and cell proliferation. Procedures for assessing these properties are described and test results are given for (E)-4-[4-(2-(3-methylcyclohexylaminocarbonyl)ethenyl)anilino]-6,7-dimethoxyquinazoline.

IT **331734-29-3P**, (E)-4-[4-(2-Carboxyethenyl)anilino]-6,7-dimethoxyquinazoline **331734-31-7P**, (E)-4-[4-(2-Carboxyethenyl)anilino]-6-methoxy-7-(2,2,2-trifluoroethoxy)quinazoline hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazoline derivs., method of preparation and use
in inhibiting aurora 2 kinase)

IT **331733-89-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinazoline derivs., method of preparation and use in inhibiting
aurora 2 kinase)

IT **331733-38-1P 331733-40-5P 331733-43-8P**
331733-44-9P 331733-46-1P 331733-48-3P
331733-50-7P 331733-52-9P 331733-53-0P
331733-55-2P 331733-57-4P 331733-59-6P
331733-61-0P 331733-64-3P 331733-68-7P
331733-71-2P 331733-75-6P 331733-77-8P
331733-79-0P 331733-80-3P 331733-81-4P
331733-82-5P 331733-84-7P 331733-85-8P
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331734-02-2P 331734-03-3P 331734-04-4P
331734-05-5P 331734-06-6P 331734-07-7P
331734-08-8P 331734-09-9P 331734-10-2P
331734-11-3P 331734-12-4P 331734-13-5P
331734-14-6P 331734-15-7P 331734-16-8P
331734-17-9P 331734-19-1P 331734-20-4P
331734-21-5P 331734-22-6P 331734-23-7P
331734-24-8P 331734-25-9P 331734-26-0P
331734-27-1P, (E)-4-[4-(2-Carboethoxyethenyl)anilino]-6,7-dimethoxyquinazoline **331734-28-2P**, (E)-4-[4-(2-Carboethoxyethenyl)phenoxy]-6,7-dimethoxyquinazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs., method of preparation and use in inhibiting
aurora 2 kinase)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Mar 2001
ACCESSION NUMBER: 2001:228864 CAPLUS
DOCUMENT NUMBER: 134:252355
TITLE: Preparation of quinazolines as aurora 2 kinase inhibitors
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021594	A1	20010329	WO 2000-GB3556	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000014133	A	20020611	BR 2000-14133	20000918
TR 200200749	T2	20020621	TR 2002-200200749	20000918
EP 1218356	A1	20020703	EP 2000-962677	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003509497	T2	20030311	JP 2001-524973	20000918
EE 200200149	A	20030415	EE 2002-149	20000918
AU 763242	B2	20030717	AU 2000-74325	20000918
ZA 2002001833	A	20030605	ZA 2002-1833	20020305
BG 106491	A	20021229	BG 2002-106491	20020307
NO 2002001401	A	20020521	NO 2002-1401	20020320
PRIORITY APPLN. INFO.:			GB 1999-22152 A	19990921
			GB 1999-22156 A	19990921
			GB 1999-22159 A	19990921
			WO 2000-GB3556 W	20000918

OTHER SOURCE(S): MARPAT 134:252355
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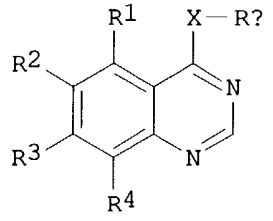

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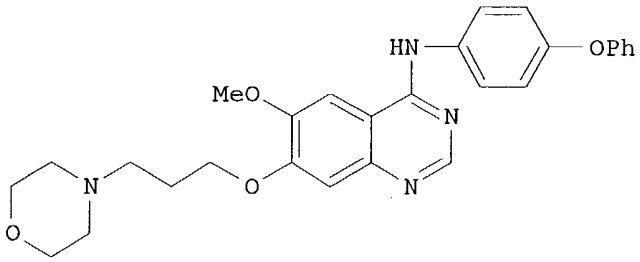

II

AB Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR8; R8 = H or alkyl; Ra = (un)substituted 3-quinolinyl or Ph; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R12, or R14X1; R12 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un)substituted NHCO, CONH, SO2NH, NHSO2, or NH; R14 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 4-phenoxyaniline•HCl and 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline were refluxed in i-PrOH to yield II (86%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.069 μM. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 2.89 μM and reduced BrdU incorporation into cellular DNA by 50% at 3.68 μM.

IT **330999-73-0**

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of 4-substituted quinazoline aurora 2 kinase inhibitors for treatment of cancer and other proliferative diseases)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'REGISTRY' ENTERED AT 11:41:27 ON 09 NOV 2004

L17 73 SEA FILE=REGISTRY ABB=ON PLU=ON (330999-73-0/BI OR 331733-38-1/BI OR 331733-40-5/BI OR 331733-43-8/BI OR 331733-44-9/BI OR 331733-46-1/BI OR 331733-48-3/BI OR 331733-50-7/BI OR 331733-52-9/BI OR 331733-53-0/BI OR 331733-55-2/BI OR 331733-57-4/BI OR 331733-59-6/BI OR 331733-61-0/BI OR 331733-64-3/BI OR 331733-68-7/BI OR 331733-71-2/BI OR 331733-75-6/BI OR 331733-77-8/BI OR 331733-79-0/BI OR 331733-80-3/BI OR 331733-81-4/BI OR 331733-82-5/BI OR 331733-84-7/BI OR 331733-85-8/BI OR 331733-86-9/BI OR 331733-87-0/BI OR 331733-88-1/BI OR 331733-89-2/BI OR 331733-90-5/BI OR 331733-91-6/BI OR 331733-92-7/BI OR 331733-93-8/BI OR 331733-94-9/BI OR 331733-95-0/BI OR 331733-96-1/BI OR 331733-97-2/BI OR 331733-98-3/BI OR 331733-99-4/BI OR 331734-00-0/BI OR 331734-01-1/BI OR 331734-02-2/BI OR 331734-03-3/BI OR 331734-04

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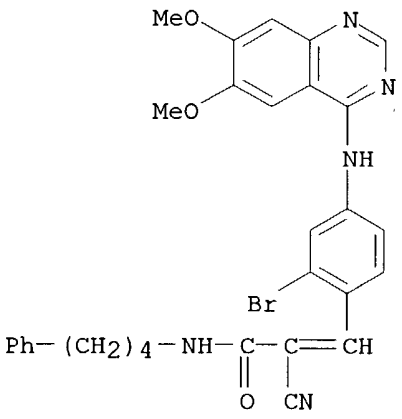
Random RNs displayed

=> d 1,4,5,15,28,36,47,52,69,73 ide can

L17 ANSWER 1 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **655248-63-8** REGISTRY
CN 2-Propenamide, 3-[2-bromo-4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-2-cyano-N-(4-phenylbutyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3-[2-Bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyano-N-(4-phenylbutyl)acrylamide
FS 3D CONCORD
MF C30 H28 Br N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



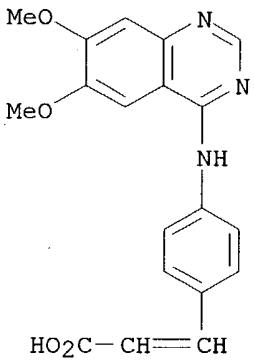
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:163886

L17 ANSWER 4 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN

RN **331776-88-6** REGISTRY
CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H17 N3 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266317

L17 ANSWER 5 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331734-31-7** REGISTRY
CN 2-Propenoic acid, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-, hydrochloride, (2E)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (E)-4-[4-(2-Carboxyethenyl)anilino]-6-methoxy-7-(2,2,2-trifluoroethoxy)quinazoline hydrochloride
FS STEREOSEARCH
MF C20 H16 F3 N3 O4 . x Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
CRN (756466-68-9)

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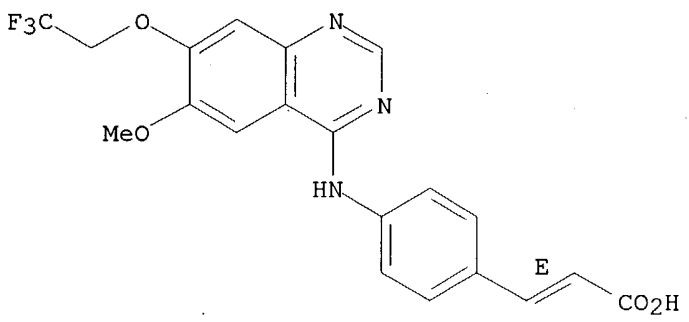

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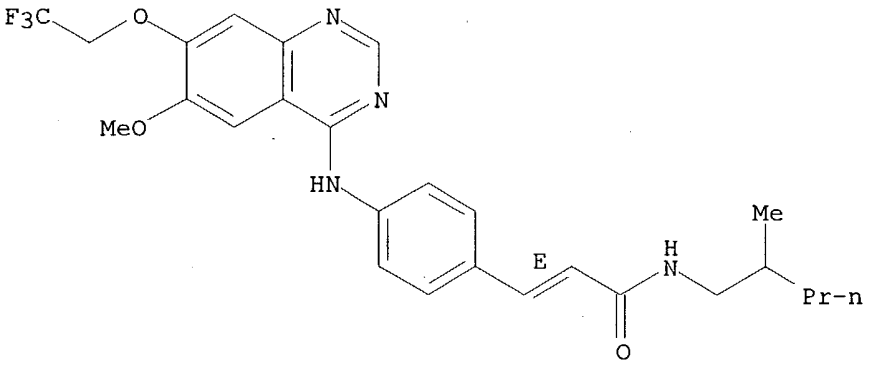
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 15 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331734-20-4** REGISTRY
CN 2-Propenamide, 3-[4-[[6-methoxy-7-(2,2,2-trifluoroethoxy)-4-quinazolinyl]amino]phenyl]-N-(2-methylpentyl)-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H29 F3 N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Double bond geometry as shown.



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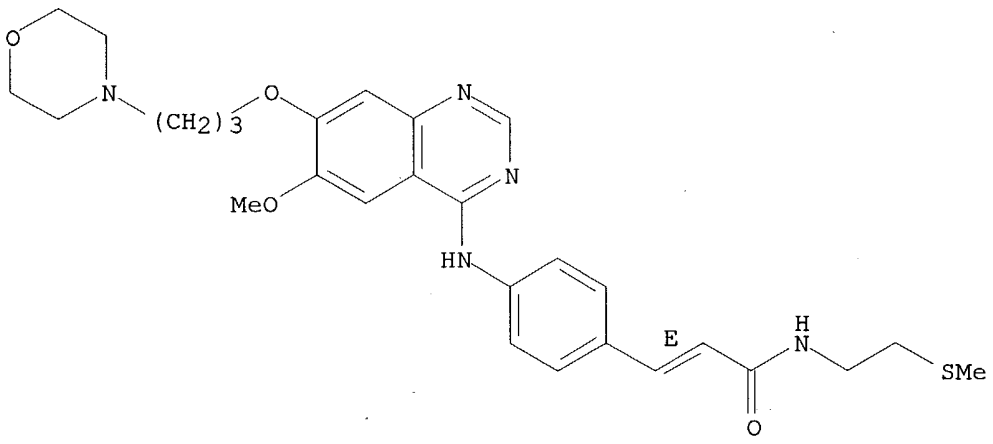
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 28 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331734-06-6** REGISTRY
CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-[2-(methylthio)ethyl]-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H35 N5 O4 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Double bond geometry as shown.



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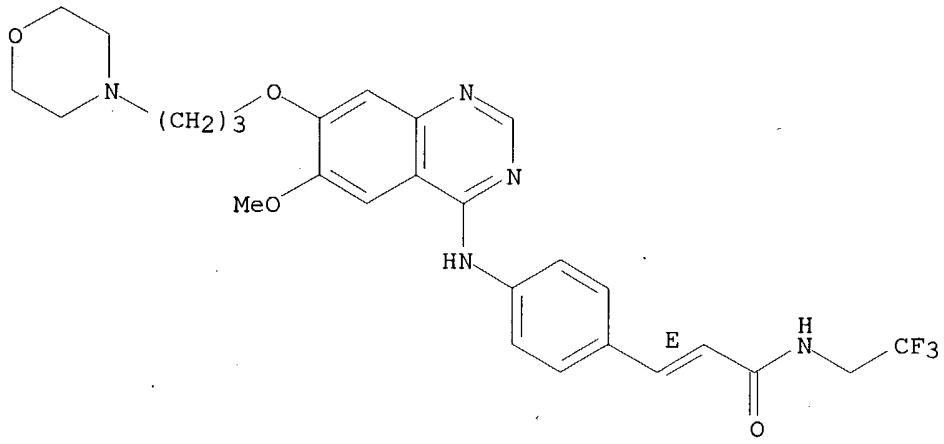
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 36 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331733-98-3** REGISTRY
CN 2-Propenamide, 3-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-N-(2,2,2-trifluoroethyl)-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H30 F3 N5 O4
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Double bond geometry as shown.



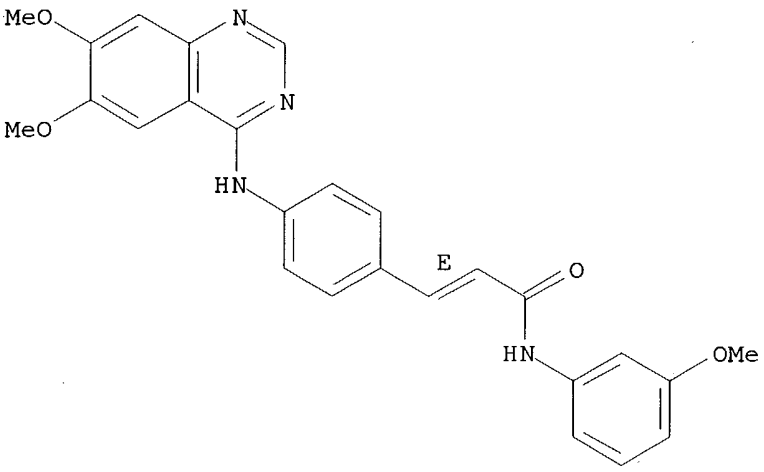
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 47 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331733-87-0** REGISTRY
CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(3-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H24 N4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Double bond geometry as shown.



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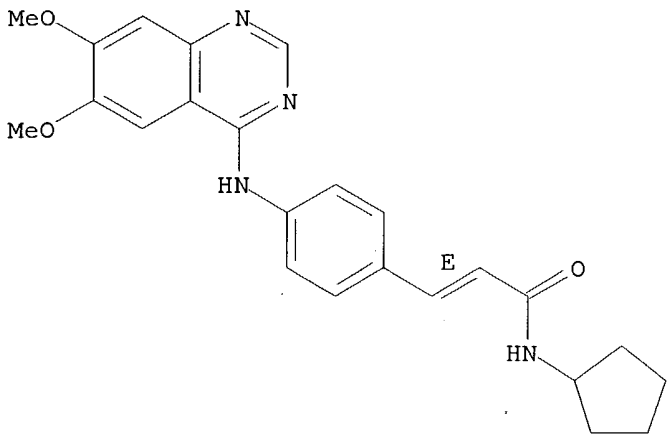
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 52 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331733-81-4** REGISTRY
CN 2-Propenamide, N-cyclopentyl-3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H26 N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Double bond geometry as shown.



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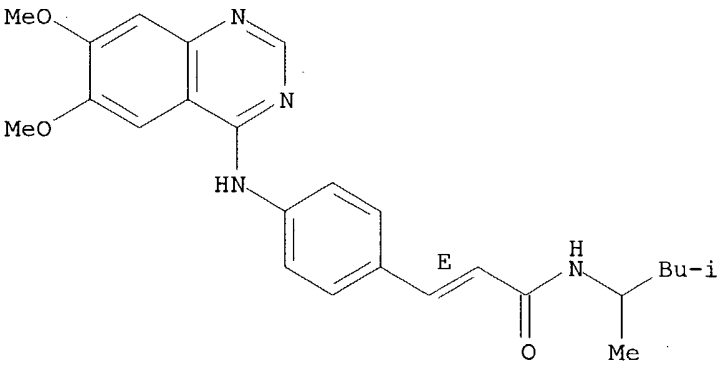
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 69 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **331733-44-9** REGISTRY
CN 2-Propenamide, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-N-(1,3-dimethylbutyl)-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H30 N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Double bond geometry as shown.



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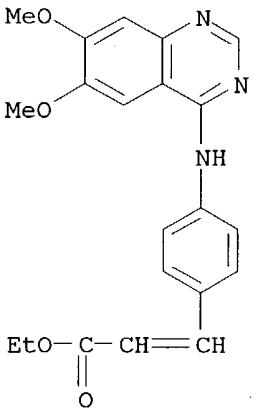
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:266316

L17 ANSWER 73 OF 73 REGISTRY COPYRIGHT 2004 ACS on STN
RN **330999-73-0** REGISTRY
CN 2-Propenoic acid, 3-[4-[(6,7-dimethoxy-4-quinazolinyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H21 N3 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: RACT (Reactant or reagent)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

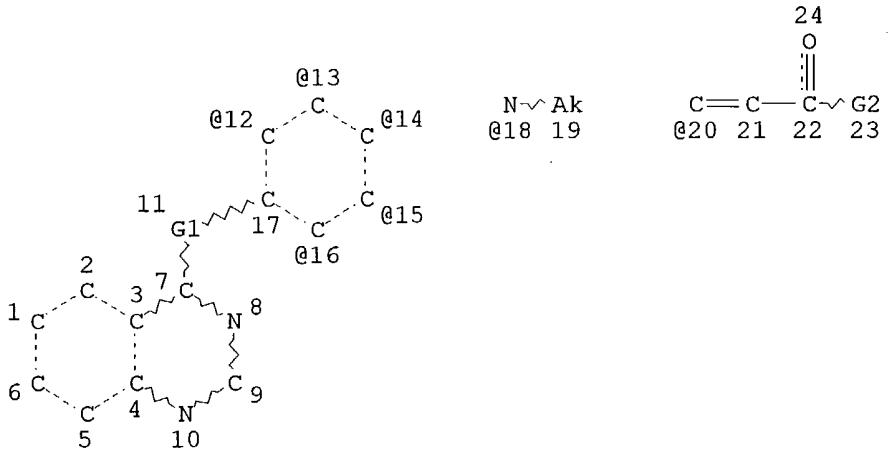
REFERENCE 1: 134:252355

FILE 'CAOLD' ENTERED AT 11:42:58 ON 09 NOV 2004
L18 0 S L17

FILE 'USPATFULL' ENTERED AT 11:43:03 ON 09 NOV 2004
L19 0 S L17

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 11:43:11 ON 09 NOV 2004
L20 0 S L17

(FILE 'MARPAT' ENTERED AT 11:43:27 ON 09 NOV 2004)
L21 STR



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CONNECT IS E2 RC AT 9
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 19
GGCAT IS LOC AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L23 5 SEA FILE=MARPAT SSS FUL L21 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 3512 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.07

L23 ANSWER 1 OF 5 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:163886 MARPAT
TITLE: Preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases
INVENTOR(S): Gazit, Aviv; Levitzki, Alexander
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013091	A2	20040212	WO 2003-IL632	20030731
WO 2004013091	A3	20040729		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-399736P 20020801

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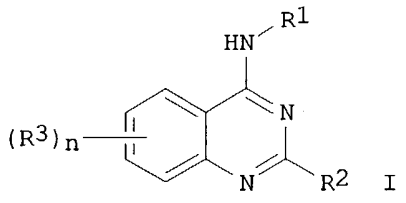

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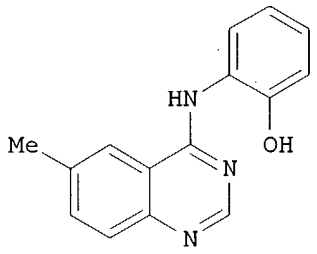

II

AB Title compds. I [R1 = (un)substituted Ph, naphthyl, etc.; R2 = H, halo, phenylamino, etc.; R3 = H, alkoxy, NO2, etc.; n = 1-3] are prepared For instance, 4-chloro-6-methylquinazoline is reacted with 2-aminophenol (EtOH, reflux, 1 h) to give II. I are potent inhibitors of protein tyrosine (PTK) kinase activity, particularly epidermal growth factor receptor (EGFR) kinase activity. I are useful in treating a variety of PTK related disorders such as cell proliferative disorders, fibrotic disorders, metabolic disorders and cancer.

IC ICM C07D

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST aniline quinazoline inhibitor epidermal growth factor receptor kinase prepn

IT Metabolism, animal
(disorder; preparation of 4-anilino substituted quinazolines as inhibitors
of epidermal growth factor receptor kinases)

IT Cell proliferation
(inhibition; preparation of 4-anilino substituted quinazolines as inhibitors
of epidermal growth factor receptor kinases)

IT Antitumor agents
Human

Neoplasm
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

IT Epidermal growth factor receptors
Fibroblast growth factor receptors
Hepatocyte growth factor receptors
Insulin-like growth factor I receptors
Macrophage colony-stimulating factor receptors
Nerve growth factor receptors
Platelet-derived growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

IT 79079-06-4, EGFR kinase 80449-02-1, Protein tyrosine kinase 88201-45-0, Insulin receptor kinase 386705-49-3, Vascular endothelial growth factor receptor kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

IT 27631-29-4P, 2,4-Dichloro-6,7-dimethoxyquinazoline 655248-11-6P, 2-Chloro-4-indolyl-6,7-dimethoxyquinazoline 655248-31-0P, 4-(3-Formylindolyl)-6,7-dimethoxyquinazoline 655248-58-1P, 4-[[3-Bromo-4-(diethoxymethyl)phenyl]amino]-6,7-dimethoxyquinazoline 655248-79-6P, 4-[4-[Carboxamido]phenylamino]-6-nitroquinazoline
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

IT 77725-90-7P, 4-[[4-[Benzyloxy]phenyl]amino]quinazoline 146871-74-1P, 4-(3-Cyanophenylamino)quinazoline hydrochloride 153437-03-7P, 4-[[3-Chloro-4-fluorophenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 153437-09-3P, 4-[[4-Fluoro-3-nitrophenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 153437-54-8P, 4-[3-Aminophenylamino]-6,7-dimethoxyquinazoline hydrochloride 169205-77-0P, 4-[3-Bromophenylamino]-6-nitroquinazoline 169205-78-1P, 4-[3-Bromophenylamino]-6-aminoquinazoline 179246-74-3P, 4-[[4-[Benzyloxy]phenyl]amino]quinazoline hydrochloride 179246-75-4P, 4-[[4-[Benzyloxy]phenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 179248-59-0P, 4-[[4-[[Phenyl]oxy]phenyl]amino]-6,7-dimethoxyquinazoline 179248-61-4P, 4-[[4-[Benzyloxy]phenyl]amino]-6,7-dimethoxyquinazoline 182480-71-3P, 4-(2-Hydroxyphenylamino)-6-methylquinazoline 182480-79-1P, 2,4-Bis(3-chlorophenylamino)-6,7-dimethoxyquinazoline 183322-30-7P, 4-[[3-Amino-5-chlorophenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 188829-39-2P, 4-[4-Hydroxyphenylamino]-6,7-dimethoxyquinazoline hydrochloride 197231-36-0P, 2-Chloro-4-(3-bromophenylamino)-6,7-dimethoxyquinazoline 263400-54-0P, 4-[3-Aminophenylamino]-6,7-dimethoxyquinazoline 296234-93-0P, 4-[[3,5-Dichloro-4-hydroxyphenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 296234-94-1P, 4-[[3-Chloro-4-hydroxyphenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 303120-53-8P, 4-(1-Naphthylamino)-6-methylquinazoline 655248-10-5P, 2-Chloro-4-indolyl-6,7-dimethoxyquinazoline hydrochloride 655248-12-7P, 2-Chloro-4-(5-nitroindolyl)-6,7-dimethoxyquinazoline hydrochloride 655248-13-8P, 2-Chloro-4-(5-nitroindolyl)-6,7-dimethoxyquinazoline 655248-14-9P, 2-Chloro-4-(6-nitroindolyl)-6,7-dimethoxyquinazoline hydrochloride 655248-15-0P, 2-Chloro-4-(6-

nitroindolyl)-6,7-dimethoxyquinazoline 655248-16-1P, 4-(4-Cyanophenylamino)quinazoline hydrochloride 655248-17-2P, 4-(4-Cyanophenylamino)quinazoline 655248-18-3P, 4-(2-Cyanophenylamino)quinazoline 655248-19-4P, 4-(2-Cyanophenylamino)-6-methylquinazoline 655248-20-7P, 4-[[2,4-Difluoro-3-chlorophenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 655248-21-8P, 4-[[2,4-Difluoro-3-chlorophenyl]amino]-6,7-dimethoxyquinazoline 655248-22-9P, 4-[[4-Fluoro-3-nitrophenyl]amino]-6,7-dimethoxyquinazoline 655248-23-0P, 4-((4-Chloro-6-methylpyrimidin-2-yl)amino)-6,7-dimethoxyquinazoline hydrochloride 655248-25-2P, 4-((4-Chloro-6-methylpyrimidin-2-yl)amino)-6,7-dimethoxyquinazoline 655248-26-3P, 4-((4-Amino-6-chlorotriazin-2-yl)amino)-6,7-dimethoxyquinazoline hydrochloride 655248-27-4P, 4-((4-Amino-6-chlorotriazin-2-yl)amino)-6,7-dimethoxyquinazoline 655248-28-5P, 4-(4-Nitrophenylamino)-6-methylquinazoline hydrochloride 655248-29-6P, 4-(3-Cyanophenylamino)-6-methylquinazoline hydrochloride 655248-30-9P, 4-[[2-Carboxy-5-chlorophenyl]amino]-6,7-dimethoxyquinazoline 655248-32-1P, 2-Cyano-N-(3,4-dimethoxyphenyl)-3-[1-(6,7-dimethoxyquinazolin-4-yl)-1H-indol-3-yl]acrylamide 655248-33-2P, 2-[[Benzothiazol-2-yl]sulfanyl]-4-indolyl-6,7-dimethoxyquinazoline 655248-34-3P, 2-[[Benzothiazol-2-yl]sulfanyl]-4-(4-methylphenylamino)-6,7-dimethoxyquinazoline 655248-35-4P, 2-[[Benzothiazol-2-yl]sulfanyl]-4-(3-chlorophenylamino)-6,7-dimethoxyquinazoline 655248-36-5P, 4-[[4-[[Phenyl]carbonyl]phenyl]amino]-6-methylquinazoline hydrochloride 655248-37-6P, 4-[[2-Phenylphenyl]amino]-6-methylquinazoline 655248-38-7P, 4-[[3-Quinolyl]amino]-6-methylquinazoline hydrochloride 655248-39-8P, 4-[[3-Quinolyl]amino]-6-methylquinazoline 655248-41-2P, 4-[[6-Indazolyl]amino]-6-methylquinazoline hydrochloride 655248-42-3P, 4-[[6-Indazolyl]amino]-6-methylquinazoline 655248-43-4P, 4-[[2-[[Phenyl]carbonyl]phenyl]amino]-6-methylquinazoline hydrochloride 655248-44-5P, 4-[[2-[[Phenyl]carbonyl]phenyl]amino]-6-methylquinazoline 655248-45-6P, 4-[[4-Chloro-2-((phenyl)carbonyl)phenyl]amino]-6-methylquinazoline hydrochloride 655248-46-7P, 4-[[4-Chloro-2-((phenyl)carbonyl)phenyl]amino]-6-methylquinazoline 655248-47-8P 655248-48-9P 655248-49-0P, 4-[(4-((4-Methoxyphenyl)carbonyl)phenyl)amino]-6-methylquinazoline hydrochloride 655248-50-3P, 4-[(4-((4-Methoxyphenyl)carbonyl)phenyl)amino]-6-methylquinazoline 655248-51-4P, 4-[(4-(Benzyloxy)phenyl)amino]-6-methylquinazoline hydrochloride 655248-52-5P, 4-[(4-(Benzyloxy)phenyl)amino]-6-methylquinazoline 655248-53-6P, 4-[(3-(Benzyloxy)phenyl)amino]-6-methylquinazoline hydrochloride 655248-54-7P, 4-[(3-(Benzyloxy)phenyl)amino]-6-methylquinazoline 655248-55-8P, 4-[[4-[Benzyloxy]phenyl]amino]-8-methylquinazoline hydrochloride 655248-56-9P, 4-[[4-[Benzyloxy]phenyl]amino]-8-methylquinazoline 655248-59-2P, 4-[[3-Bromo-4-formylphenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 655248-60-5P, 4-[[3-Bromo-4-formylphenyl]amino]-6,7-dimethoxyquinazoline 655248-61-6P, 3-[2-Bromo-4-((6,7-dimethoxyquinazoline-4-yl)amino)phenyl]-2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]acrylamide 655248-62-7P, N-Benzyl-3-[2-bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyanoacrylamide 655248-63-8P, 3-[2-Bromo-4-((6,7-dimethoxyquinazolin-4-yl)amino)phenyl]-2-cyano-N-(4-phenylbutyl)acrylamide 655248-64-9P, 4-[[3-Amino-5-(carbomethoxy)phenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 655248-65-0P, 4-[[3-Amino-5-(carbomethoxy)phenyl]amino]-6,7-dimethoxyquinazoline 655248-66-1P, 4-[[3-Chloro-5-(carbomethoxy)phenyl]amino]-6,7-dimethoxyquinazoline 655248-67-2P, 4-[[3-((Piperidin-1-yl)azo)phenyl]amino]-6,7-dimethoxyquinazoline

655248-68-3P, 4-[4-(Carboxamido)phenylamino]-6,7-dimethoxyquinazoline hydrochloride 655248-69-4P, 4-[3-(Carboxamido)phenylamino]-6,7-dimethoxyquinazoline hydrochloride 655248-70-7P, 4-[3-Amino-5-chlorophenylamino]-6-methylquinazoline hydrochloride 655248-71-8P, 4-[[3,5-Dibromo-4-hydroxyphenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 655248-72-9P, 4-[[4-[[4-Aminophenyl]oxy]phenyl]amino]-6,7-dimethoxyquinazoline 655248-73-0P, 4-[4-(Carboxamido)phenylamino]-6-methylquinazoline hydrochloride 655248-74-1P, 4-[4-(Carboxamido)phenylamino]-6-methylquinazoline 655248-75-2P, 4-[[4-(Carboethoxy)phenyl]amino]-6,7-dimethoxyquinazoline hydrochloride 655248-76-3P, 4-[[4-(Carboethoxy)phenyl]amino]-6,7-dimethoxyquinazoline 655248-77-4P, 4-[4-(Acetyl)phenylamino]-6,7-dimethoxyquinazoline hydrochloride 655248-78-5P, 4-[4-[Carboxamido]phenylamino]-6-nitroquinazoline hydrochloride 655248-80-9P, 4-[4-[Carboxamido]phenylamino]-6-aminoquinazoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

IT 56-41-7, Alanine, reactions 75-12-7, Formamide, reactions 90-41-5, 2-Aminobiphenyl 94-09-7, Ethyl 4-aminobenzoate 95-55-6, 2-Aminophenol 99-92-3 100-01-6, p-Nitroaniline, reactions 101-80-4, 4,4'-Oxydianiline 108-45-2, 1,3-Phenylenediamine, reactions 123-30-8, 4-Hydroxyaniline 134-32-7, 1-Aminonaphthalene 139-59-3, 4-Phenoxyaniline 149-30-4, 2-Mercaptobenzothiazole 364-76-1, 3-Nitro-4-fluoroaniline 367-21-5, 3-Chloro-4-fluoroaniline 487-89-8, 3-Formylindole 496-15-1, Indoline 580-17-6, 3-Aminoquinoline 591-19-5, 3-Bromoaniline 607-68-1, 2,4-Dichloroquinazoline 609-21-2, 4-Hydroxy-3,5-dibromoaniline 616-79-5, 5-Nitroanthranilic acid 873-74-5, 4-Cyanoaniline 1137-41-3, 4-Aminobenzophenone 1885-29-6, 2-Cyanoaniline 1949-55-9, 5-Carbomethoxy-1,3-phenylenediamine 2237-30-1, m-Cyanoaniline 2613-34-5, 2,4-Difluoro-3-chloroaniline 2835-68-9, 4-(Carboxamido)aniline 2835-77-0, 2-Aminobenzophenone 3397-62-4, 2,4-Diamino-6-chlorotriazine 3544-24-9, 3-(Carboxamido)aniline 3586-12-7, 3-Phenoxyaniline 3964-52-1, 3-Chloro-4-hydroxyaniline 4076-50-0, 2-Amino-4-chlorobenzophenone 4834-72-4, 4-Amino-4'-methoxybenzophenone 5190-68-1, 4-Chloroquinazoline 5600-21-5 5930-28-9, 4-Hydroxy-3,5-dichloroaniline 6388-47-2, 2-Amino-3-chlorobenzoic acid 6967-12-0, 6-Aminoindazole 13790-39-1, 4-Chloro-6,7-dimethoxyquinazoline 19727-83-4, 6-Nitroindoline 21961-31-9, 5-Carbomethoxy-3-chloroaniline 28888-44-0, 6,7-Dimethoxy-2,4-quinazolinedione 32692-19-6, 5-Nitroindoline 33786-89-9, 5-Chloro-1,3-phenylenediamine 58421-79-7, 4-Chloro-6-methylquinazoline 58421-80-0, 4-Chloro-8-methylquinazoline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

IT 6943-17-5P 19815-16-8P 655248-57-0P, 3-Bromo-4-formylaniline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-anilino substituted quinazolines as inhibitors of epidermal growth factor receptor kinases)

L23 ANSWER 2 OF 5 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:266316 MARPAT

TITLE: Preparation of quinazoline derivatives, method of preparation and use in inhibiting aurora 2 kinase
INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021595	A1	20010329	WO 2000-GB3562	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000014136	A	20020521	BR 2000-14136	20000918
EP 1218357	A1	20020703	EP 2000-962682	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003509498	T2	20030311	JP 2001-524974	20000918
EE 200200148	A	20030415	EE 2002-148	20000918
ZA 2002001831	A	20030605	ZA 2002-1831	20020305
NO 2002001395	A	20020515	NO 2002-1395	20020320
BG 106535	A	20021229	BG 2002-106535	20020320
PRIORITY APPLN. INFO.:			GB 1999-22173	19990921
			WO 2000-GB3562	20000918

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB I or a salt, ester, amide or prodrug thereof, a method for the preparation of I and the use of the claimed compds. for inhibiting aurora 2 kinase are claimed. These compds. are useful in the treatment of cancer. In I: X is O, or S, S(O) or S(O)2 or NR10 where R10 is H or C1-6 alkyl. R5 is OR11, NR12R13 or SR11 where R11, R12 and R13 are independently optionally substituted hydrocarbyl or optionally substituted heterocyclic groups, and R12 and R13 may addnl. form together with the N atom to which they are attached, an optionally substituted aromatic or nonarom. heterocyclic ring which may contain further heteroatoms. R6 and R7 are independently H or hydrocarbyl. R8 and R9 are independently H, halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkoxymethyl, di(C1-4alkoxy)methyl, C1-4 alkanoyl, trifluoromethyl, cyano, amino, C2-5 alkenyl, C2-5 alkynyl, a Ph group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be

aromatic or nonarom. and may be saturated (linked via a ring C or N atom) or unsatd. (linked via a ring C atom), and which Ph, benzyl or heterocyclic group may bear on one or more ring C atoms up to 5 substituents selected from hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C2-4 alkanoyl, C1-4 alkanoylamino, C1-4 alkoxycarbonyl, C1-4 alkylthio, C1-4 alkylsulfinyl, C1-4 alkylsulfonyl, carbamoyl, N-C1-4alkylcarbamoyl, N,N-di(C1-4alkyl)carbamoyl, aminosulfonyl, N-C1-4alkylaminosulfonyl, N,N-di(C1-4alkyl)aminosulfonyl, C1-4 alkylsulfonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C1-4alkoxycarbonyl. R1, R2, R3, R4 are independently halo, cyano, nitro, C1-3 alkylthio, -N(OH)R14 (R14 is H, or C1-3 alkyl), or R16X1- (X1 represents a direct bond, -O-, -CH2-, -OC(O)-, -C(O)-, -S-, -SO-, -SO2-, -NR17C(O)-, -C(O)NR18-, -SO2NR19-, -NR20SO2- or -NR21- (R17, R18, R19, R20 and R21 each independently represents H, C1-3 alkyl or C1-3alkoxyC2-3alkyl), and R16 is H, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy). A method for preparing I comprises reacting II where X, R8 and R9 are as defined above, R1', R2', R3', R4' are groups R1, R2, R3, R4 as defined above resp., or precursors thereof; and R85 is a leaving group, with HCR6:CR7C(O)R5', where R6 and R7 are as defined above, R5' is a group R5 as defined above or a precursor group therefore; and thereafter if desired or necessary, converting any precursor groups R1', R2', R3', R4' or R5' to groups R1, R2, R3, R4 or R5 resp., or changing a group R5 to a different such group. The compds. of the invention inhibit the serine/threonine kinase activity of the aurora 2 kinase and thus inhibit the cell cycle and cell proliferation. Procedures for assessing these properties are described and test results are given for (E)-4-[4-(2-(3-methylcyclohexylaminocarbonyl)ethenyl)anilino]-6,7-dimethoxyquinazoline.

IC ICM C07D239-94
ICS A61K031-517; A61P035-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST quinazoline deriv prepn method inhibition aurora 2 kinase; antitumor agent quinazoline deriv

IT Drug delivery systems
(for quinazoline derivs. as inhibitors of aurora 2 kinase)

IT Antitumor agents
(preparation of quinazoline derivs. as)

IT 7357-67-7P, N-(3-Chloropropyl)morpholine 13790-39-1P, 4-Chloro-6,7-dimethoxyquinazoline 13794-72-4P, 6,7-Dimethoxy-3,4-dihydroquinazolin-4-one 35283-08-0P, Ethyl 3-(4-nitrophenyl)propiolate 108479-25-0P, Ethyl 3-methoxy-4-(3-morpholinopropoxy)benzoate 162364-72-9P, 4-Chloro-6-methoxy-7-benzyloxyquinazoline 168835-91-4P, 4-(4-Iodoanilino)-6,7-dimethoxyquinazoline 179688-01-8P, 7-Benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one 196194-62-4P, 6-Methoxy-7-(3-morpholinopropoxy)-3,4-dihydroquinazolin-4-one 196195-13-8P, 4-Chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline 330999-39-8P, 4-(4-Iodophenoxy)-6,7-dimethoxyquinazoline 330999-79-6P, 4-Chloro-6-methoxy-7-(2,2,2-trifluoroethoxy)quinazoline 330999-80-9P, Ethyl 4-(2,2,2-trifluoroethoxy)-3-methoxybenzoate 330999-81-0P, Ethyl 3-methoxy-4-(2,2,2-trifluoroethoxy)-6-nitrobenzoate 330999-82-1P, Ethyl

3-methoxy-4-(2,2,2-trifluoroethoxy)-6-aminobenzoate 330999-83-2P, 6-Methoxy-7-(2,2,2-trifluoroethoxy)-3,4-dihydroquinazolin-4-one 330999-84-3P, Ethyl 3-methoxy-4-(3-morpholinopropoxy)-6-nitrobenzoate 330999-85-4P, Ethyl 3-methoxy-4-(3-morpholinopropoxy)-6-aminobenzoate 331734-29-3P, (E)-4-[4-(2-Carboxyethenyl)anilino]-6,7-dimethoxyquinazoline 331734-31-7P, (E)-4-[4-(2-Carboxyethenyl)anilino]-6-methoxy-7-(2,2,2-trifluoroethoxy)quinazoline hydrochloride 331734-33-9P, cis-Ethyl 4-aminocinnamate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinazoline derivs., method of preparation and use
in inhibiting aurora 2 kinase)

IT 233599-27-4, Aurora 2 kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of quinazoline derivs., method of preparation and use in inhibiting)

IT 331733-89-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinazoline derivs., method of preparation and use in inhibiting
aurora 2 kinase)

IT 331733-38-1P 331733-40-5P 331733-41-6P 331733-43-8P 331733-44-9P
331733-46-1P 331733-48-3P 331733-50-7P 331733-52-9P 331733-53-0P
331733-55-2P 331733-57-4P 331733-59-6P 331733-61-0P 331733-64-3P
331733-68-7P 331733-71-2P 331733-75-6P 331733-77-8P 331733-79-0P
331733-80-3P 331733-81-4P 331733-82-5P 331733-83-6P 331733-84-7P
331733-85-8P 331733-86-9P 331733-87-0P 331733-88-1P 331733-90-5P
331733-91-6P 331733-92-7P 331733-93-8P 331733-94-9P 331733-95-0P
331733-96-1P 331733-97-2P 331733-98-3P 331733-99-4P 331734-00-0P
331734-01-1P 331734-02-2P 331734-03-3P 331734-04-4P 331734-05-5P
331734-06-6P 331734-07-7P 331734-08-8P 331734-09-9P 331734-10-2P
331734-11-3P 331734-12-4P 331734-13-5P 331734-14-6P 331734-15-7P
331734-16-8P 331734-17-9P 331734-19-1P 331734-20-4P 331734-21-5P
331734-22-6P 331734-23-7P 331734-24-8P 331734-25-9P 331734-26-0P
331734-27-1P, (E)-4-[4-(2-Carboethoxyethenyl)anilino]-6,7-dimethoxyquinazoline 331734-28-2P, (E)-4-[4-(2-Carboethoxyethenyl)phenoxy]-6,7-dimethoxyquinazoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs., method of preparation and use in inhibiting
aurora 2 kinase)

IT 62-53-3, Aniline, reactions 78-81-9, Isobutylamine 89-97-4, 2-Chlorobenzylamine 90-04-0, 2-Methoxyaniline 95-53-4, 2-Methylaniline, reactions 100-46-9, Benzylamine, reactions 106-47-8, 4-Chloroaniline, reactions 106-49-0, 4-Methylaniline, reactions 108-09-8, 1,3-Dimethylbutylamine 108-44-1, 3-Methylaniline, reactions 108-91-8, Cyclohexylamine, reactions 109-55-7, 3-(Dimethylamino)propylamine 109-70-6, 1-Bromo-3-chloropropane 109-73-9, n-Butylamine, reactions 109-85-3, 2-Methoxyethylamine 110-89-4,

Piperidine, reactions 110-91-8, Morpholine, reactions 140-88-5, Ethyl acrylate 373-88-6, 2,2,2-Trifluoroethylamine hydrochloride 462-08-8, 3-Aminopyridine 504-29-0, 2-Aminopyridine 536-90-3, 3-Methoxyaniline 540-37-4, 4-Iodoaniline 540-38-5, 4-Iodophenol 557-66-4, Ethylamine hydrochloride 616-30-8, 3-Amino-1,2-propanediol 617-05-0, Ethyl vanillate 617-89-0, Furfurylamine 623-47-2, Ethyl propiolate 636-98-6, 4-Iodonitrobenzene 765-30-0, Cyclopropylamine 1003-03-8, Cyclopentylamine 2338-18-3, 2-Aminoindan hydrochloride 2450-71-7, Propargylamine 2516-34-9, Cyclobutylamine 2975-41-9, 2-Aminoindan 3218-02-8, Cyclohexanemethanamine 4795-29-3, Tetrahydrofurfurylamine 5350-93-6, 5-Amino-2-chloropyridine 5653-40-7, 4,5-Dimethoxyanthranilic acid 6338-70-1, 3-Aminotetrahydrothiophene-1,1'-dioxide 6850-35-7, 3-Methylcyclohexylamine 13364-16-4, 2-Methyl-1-amylamine 14003-16-8, 5-Methyl-2-(aminomethyl)furan 17570-30-8, (E)-4-Aminocinnamic acid 18542-42-2, 2-(Methylthio)ethylamine 30433-91-1, 2-Thiophene ethylamine 37143-54-7, 2-Amino-1-methoxypropane 60547-98-0, 2-Amino-4-benzyloxy-5-methoxybenzamide 97306-73-5, 4-Chlorotetrahydro-3-thiophenamine-1,1-dioxide hydrochloride 139223-62-4, (E)-4-Aminocinnamic acid hydrochloride 198195-25-4, (E)-Ethyl 4-aminocinnamate 331734-30-6, 3-Aminotetrahydrothiophene-1,1'-dioxide dihydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of quinazoline derivs., method of preparation and use in
inhibiting aurora 2 kinase)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 5 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 134:29705 MARPAT
TITLE: Preparation of squaric acid derivatives as cell adhesion molecules
INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrelow, Graham John
PATENT ASSIGNEE(S): Celltech Chiroscience Limited, UK
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073260	A1	20001207	WO 2000-GB2020	20000526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6518283	B1	20030211	US 2000-579317	20000525

CA 2375218	AA	20001207	CA 2000-2375218	20000526
EP 1181266	A1	20020227	EP 2000-935341	20000526
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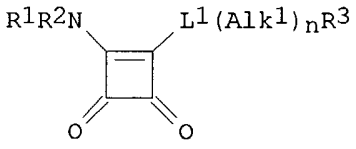
JP 2003500467	T2	20030107	JP 2000-621327	20000526
AU 776704	B2	20040916	AU 2000-50889	20000526
US 2003162799	A1	20030828	US 2002-319272	20021213
PRIORITY APPLN. INFO.:			GB 1999-12640	19990528
			GB 2000-2858	20000208
			US 2000-579317	20000525
			WO 2000-GB2020	20000526

GI



I

AB Squaric acid derivs. I [R1 is an integrin binding group; R2 is a hydrogen atom or a C1-6 alkyl group; L1 is a covalent bond or a linker atom or group; n = 0, 1; Alk1 is an optionally substituted aliphatic chain; R3 is H or an optionally substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., polyheterocycloaliph., aromatic or heteroarom. group] and their salts, solvates, hydrates and N-oxides were prepared as inhibitors of the binding of integrins to their ligands. Thus, treatment of Et (S)-3-(4-aminophenyl)-2-(tert-butoxycarbonylamino)propionate with 3,5-dichloro-4-pyridinecarboxylic acid, deprotection, reaction with 3,4-diisopropoxy-3-cyclobutene-1,2-dione, propylamination, and saponification afforded (S)-3-[4-(3,5-dichloro-4-pyridylcarboxamido)phenyl]-2-(2-propylamino-3,4-dioxocyclobut-1-enylamino)propanoic acid. Compds. of the invention in which R1 is an α4 integrin binding group generally have IC50 values <1 μM in the α4β1 and α4β7 assays.

IC ICM C07C229-36
ICS C07C271-28; C07C229-34; C07C271-22; C07C233-81; C07C235-16; C07C235-84; C07C235-64; C07C233-55; C07C255-57; C07C235-56; C07C271-58; C07C237-40; C07D295-12; C07D213-81; C07D213-79; C07D471-04; C07D333-70; C07D239-42; C07D215-42

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 24

ST squaric acid amino prepn cell adhesion; aminosquaric acid prepn cell adhesion; integrin inhibitor squaric acid deriv; aminopropanoic squaric acid deriv prepn cell adhesion

IT Cell adhesion
Platelet aggregation inhibitors
(preparation of squaric acid derivs. as cell adhesion mols.)

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT Integrins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT 312292-12-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(Preparation of squaric acid derivs. as cell adhesion mols.)

IT 312292-13-0P 312292-15-2P 312292-17-4P 312292-19-6P 312292-21-0P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT 312292-14-1P 312292-16-3P 312292-18-5P 312292-20-9P 312292-22-1P
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312294-71-6P 312294-72-7P 312294-73-8P 312294-74-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT 312294-75-0P 312294-76-1P 312294-77-2P 312294-78-3P 312294-79-4P
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312295-30-0P 312295-31-1P 312295-32-2P 312295-33-3P 312295-34-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT 61-54-1, 2 3 Indolyl ethylamine 62-23-7, 4-Nitrobenzoic acid 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions 78-81-9, Isobutylamine 88-14-2, 2-Furoic acid 96-15-1, 2-Methylbutylamine 98-97-5, 2-Pyrazinecarboxylic acid 100-09-4, 4-Methoxybenzoic acid 100-46-9, Benzylamine, reactions 102-49-8, 3,4-Dichlorobenzylamine 103-67-3, n-Benzylmethylamine 103-80-0, Phenylacetyl chloride 107-10-8, Propylamine, reactions 107-11-9, Allylamine 107-85-7, Isopentylamine 108-09-8, 1,3-Dimethylbutylamine 108-91-8, Cyclohexylamine, reactions 109-55-7, 3 Dimethylamino propylamine 109-73-9, Butylamine, reactions 109-85-3, 2-Methoxyethylamine 109-89-7, Diethylamine, reactions 110-58-7, Pentylamine 110-68-9, n-Methylbutylamine 110-85-0, Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 111-92-2, Dibutylamine 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 124-02-7, Diallylamine 140-31-8, 1-Piperazineethanamine 142-84-7, Dipropylamine 156-87-6, 3-Hydroxypropylamine 403-43-0, 4-Fluorobenzoyl chloride 455-24-3, 4-Trifluoromethylbenzoic acid 456-22-4, 4-Fluorobenzoic acid 460-39-9, 3,3,3-Trifluoropropylamine 486-73-7, 1-Isoquinolinecarboxylic acid 496-41-3, 2-Benzofurancarboxylic acid 504-78-9, Thiazolidine 506-59-2, Dimethylamine hydrochloride 527-72-0, 2-Thiophenecarboxylic acid 556-08-1, 4-Acetamidobenzoic acid 557-66-4, Ethylamine hydrochloride 586-75-4, 4-Bromobenzoyl chloride 586-89-0, 4-Acetylbenzoic acid 589-08-2 593-51-1, Methylamine hydrochloride 619-65-8, 4-Cyanobenzoic acid 624-78-2, n-Ethylmethylamine 627-35-0, n-Methylpropylamine 627-37-2, n-Methylallylamine 693-05-0 760-84-9, L-Leucine hydrochloride 765-30-0, Cyclopropylamine 768-94-5,

1-Adamantylamine 937-62-2, p-Tolyl chloroformate 1007-54-1 1467-70-5
1885-14-9, Phenyl chloroformate 2038-03-1, 4-Morpholineethanamine
2038-57-5, Benzenepropanamine 2051-28-7, Decahydroquinoline 2403-22-7,
n-Benzylbutylamine 2450-71-7, 2-Propynylamine 2516-34-9,
Cyclobutylamine 2516-47-4, Cyclopropanemethanamine 2524-67-6,
4-Morpholinoaniline 2620-50-0, Piperonylamine 2906-12-9,
3-Isopropoxypropylamine 3535-37-3, 3,4-Dimethoxybenzoyl chloride
3731-51-9, 2-Pyridinemethanamine 3731-52-0, 3-Pyridinemethanamine
3731-53-1, 4 Aminomethyl pyridine 4100-13-4, 1,2,3-Thiadiazole-4-
carboxylic acid 4326-36-7 4376-18-5, 2-Methoxycarbonylbenzoic acid
4498-67-3, 3-Indazolecarboxylic acid 4659-45-4, 2,6-Dichlorobenzoyl
chloride 4747-21-1, Methylisopropylamine 5036-48-6,
n-(3-Aminopropyl)imidazole 5271-67-0, 2-Thiophenecarbonyl chloride
5308-25-8, 1-Ethylpiperazine 5317-32-8, 1-Piperazinepropanol
5332-73-0, 3-Methoxypropylamine 5334-40-7, 4-Nitro-3-pyrazolecarboxylic
acid 5638-76-6 6000-43-7, Glycine hydrochloride 6057-90-5,
β-Alanine hydrochloride 6068-72-0, 4-Cyanobenzoyl chloride
6269-89-2 6291-85-6, 3-Ethoxypropylamine 6373-50-8,
4-Cyclohexylaniline 6484-25-9, 4-Chloro-2-phenylquinazoline 7154-73-6,
1-Pyrrolidineethanamine 7169-07-5, 2,3,4-Trimethoxybenzoyl chloride
7663-77-6, 2-Pyrrolidinone, 1-(3-aminopropyl)- 7693-41-6,
4-Methoxyphenyl chloroformate 7693-46-1, 4-Nitrophenyl chloroformate
13214-66-9, Benzenebutanamine 13602-12-5, 4-Pyridinecarboxylic acid
n-oxide 13952-84-6, 1-Methylpropylamine 15673-00-4,
3,3-Dimethylbutylamine 15733-83-2, 4-Methoxy-2-quinolinecarboxylic acid
17082-09-6, trans-Cinnamoyl chloride 17498-50-9, L-Valine hydrochloride
17515-74-1 17585-69-2, L-Phenylalanine hydrochloride 18212-21-0
18213-77-9, 1-Methyl-5-nitro-4-pyrazolecarboxylic acid 18542-42-2, 2
Methylthio ethylamine 18638-99-8, 3,4,5-Trimethoxybenzylamine
19771-63-2 20984-81-0 21900-37-8, 2,6-Dimethylbenzoyl chloride
22572-33-4 23806-24-8 24065-33-6, 5-Chloro-2-thiophenecarboxylic acid
26177-43-5, 3-Nitrobenzylamine hydrochloride 27578-60-5,
1-Piperidineethanamine 27757-85-3, 2-Thiophenemethanamine 29968-78-3
30006-04-3, 2-Acetyl-3-thiophenecarboxylic acid 33403-97-3, 4
Ethylaminomethyl pyridine 37497-65-7, 1,2,3,4-Tetrahydropyridine
38377-38-7, 4-Fluorophenyl chloroformate 38496-18-3,
2,6-Dichloronicotinic acid 39828-35-8, 2,4-Dimethoxybenzoyl chloride
42132-09-2 49609-84-9, 2-Chloronicotinoyl chloride 50541-93-0
53137-27-2, 2,4-Dimethyl-5-thiazolecarboxylic acid 54150-57-1,
Benzoyloxyacetyl chloride 56671-28-4 58574-03-1 58757-38-3,
6-Chloronicotinoyl chloride 61699-62-5 63126-47-6 63493-28-7,
1-Methylbutylamine 65615-90-9 98593-51-2 99924-18-2 132883-44-4
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RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT 1722-12-9P, 2-Chloropyrimidine 2457-47-8P, 3,5-Dichloropyridine
3473-63-0P, Formamidine acetate 4389-50-8P, 6-Methylanthranilic acid
5222-73-1P 5231-88-9P 6575-25-3P 13790-39-1P, 4-Chloro-6,7-
dimethoxyquinazoline 13958-93-5P 19493-44-8P, 1-Chloroisoquinoline
27631-29-4P, 2,4-Dichloro-6,7-dimethoxyquinazoline 38235-77-7P
67630-01-7P 73287-85-1P 75844-41-6P 80866-88-2P 80935-77-9P,
2,6-Naphthyridin-1(2H)-one 80935-78-0P, 1-Chloro-2,6-naphthyridine
90272-82-5P 102683-52-3P 113850-76-3P 175278-17-8P,
2-Bromo-4-trifluoromethoxyaniline 177966-66-4P 179246-09-4P

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of squaric acid derivs. as cell adhesion mols.)

IT 273920-31-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of squaric acid derivs. as cell adhesion mols.)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 5 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 132:222659 MARPAT
TITLE: Preparation of aminoalkylphosphonic ester derivatives as cell adhesion inhibitors
INVENTOR(S): Kono, Yasushi; Sawada, Takayuki; Nomura, Masahiro; Takahashi, Yukie; Tsubuki, Takeshi; Sakoe, Yasuhiko; Kuriyama, Kazuhiko
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015645	A1	20000323	WO 1999-JP4913	19990910
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 9956485	A1	20000403	AU 1999-56485	19990910
PRIORITY APPLN. INFO.:			JP 1998-258841	19980911
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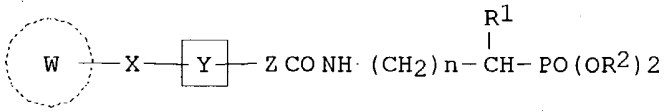

I

AB Phosphonic ester derivs. represented by general formula [I; W = thiazole ring, (un)substituted benzothiazole, pyridothiazole, pyridine, quinoline, pyridazine, phthalazine, quinoxaline, pyrimidine, quinazoline, thienopyrimidine, benzimidazole, purine, or indole ring; X = NH(CH2)m (wherein m = 0-2), CONH; Y = (un)substituted benzene, or naphthalene, pyridine, or quinoline, or benzofuran, coumarin, chroman, or chromanone, 1,3-thiazole ring; Z = (CH2)q (wherein q = 0-2), CH:CH, OCH2, OCMe2, SCH2, SOCH2, SO2CH2, NHCO(CH2)r (wherein r = 02); R1 = H, C1-4 alkoxycarbonyl, CO2H, C1-4 alkoxyphosphoryl; R2 = C1-4 alkyl; n = 0-2] and pharmacol. acceptable salts thereof are prepared These compds. have an activity of inhibiting a ICAM-1 or VCAM-1 mediated binding of cell adhesion mols. without inhibiting the expression of cell adhesion mols. and thus, are useful as immunosuppressants, anti-inflammatory agents, antiallergic agents and tumor metastasis inhibitors. Thus, 4'-(benzothiazol-2-yl)cinnamic acid was condensed with aminomethanephosphonic acid di-Et ester using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in the presence of 4-dimethylaminopyridine and Et3N in DMF at room temperature for 10 h to give [4'-(benzothiazol-2-yl)cinnamoyl]aminomethanephosphonic di-Et ester. A title compound (II) in vitro inhibited by 88% the binding of U937 cell to human umbilical vein endothelial cells (HUVEC) which were treated with human interleukin-1β to induce ICAM-1 and VCAM-1.

IC ICM C07F009-572
ICS C07F009-58; C07F009-6503; C07F009-6509; C07F009-6539; C07F009-6541; C07F009-6558; C07F009-6561; A61K031-66

CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 1

ST aminoalkylphosphonic ester prepn cell adhesion inhibitor; thiazole contg aminoalkylphosphonic ester prepn immunosuppressant; benzothiazole contg aminoalkylphosphonic ester prepn antiinflammatory; pyridothiazole contg aminoalkylphosphonic ester prepn tumor metastasis inhibitor; pyridine contg aminoalkylphosphonic ester prepn allergy inhibitor; quinoline contg aminoalkylphosphonic ester prepn; pyridazine contg aminoalkylphosphonic ester prepn; phthalazine contg aminoalkylphosphonic ester prepn; quinoxaline contg aminoalkylphosphonic ester prepn; pyrimidine contg aminoalkylphosphonic ester prepn; quinazoline contg aminoalkylphosphonic ester prepn; thienopyrimidine contg aminoalkylphosphonic ester prepn; benzimidazole contg aminoalkylphosphonic ester prepn; purine contg aminoalkylphosphonic ester prepn; indole contg aminoalkylphosphonic ester prepn

IT Antitumor agents
(metastasis; preparation of aminoalkylphosphonic ester derivs. as cell adhesion inhibitors and drugs)

IT Allergy inhibitors
Anti-inflammatory agents
Cell adhesion
Immunosuppressants
(preparation of aminoalkylphosphonic ester derivs. as cell adhesion inhibitors and drugs)

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of aminoalkylphosphonic ester derivs. as cell adhesion inhibitors and drugs)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoalkylphosphonic ester derivs. as cell adhesion inhibitors and drugs)

IT 98-88-4, Benzoyl chloride 615-20-3, 2-Chlorobenzothiazole 619-89-6, 4-Nitrocinnamic acid 638-07-3, 4-Chloroacetoacetic acid ethyl ester 1762-95-4, Ammonium thiocyanate 2182-80-1, 4-(Benzothiazol-2-yl)benzaldehyde 2393-18-2, 4-Aminocinnamic acid 2536-91-6, 2-Amino-6-methylbenzothiazole 3507-18-4 5326-23-8, 2-Chloropyridine-5-carboxylic acid 16017-69-9 16112-21-3, 2-(p-Tolyl)benzothiazole 20485-38-5 50917-72-1 52112-82-0 198195-25-4 261617-27-0 261617-31-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoalkylphosphonic ester derivs. as cell adhesion

inhibitors and drugs)
IT 532-55-8P, Benzoyl isothiocyanate 24239-18-7P, 2-(4-Bromomethylphenyl)benzothiazole 52112-81-9P 261348-95-2P 261348-96-3P 261348-97-4P 261348-98-5P 261617-24-7P 261617-25-8P 261617-26-9P 261617-28-1P 261617-29-2P 261617-30-5P 261617-32-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoalkylphosphonic ester derivs. as cell adhesion inhibitors and drugs)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 5 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 132:222544 MARPAT
TITLE: Preparation of malonic diester derivatives as cell adhesion inhibitors and process for producing the same
INVENTOR(S): Kono, Yasushi; Nomura, Masahiro; Sawada, Takayuki; Ando, Naoki; Takahashi, Yukie; Kuriyama, Kazuhiko
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015604	A1	20000323	WO 1999-JP4914	19990910
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9956486	A1	20000403	AU 1999-56486	19990910
PRIORITY APPLN. INFO.:			JP 1998-258840	19980911
			WO 1999-JP4914	19990910

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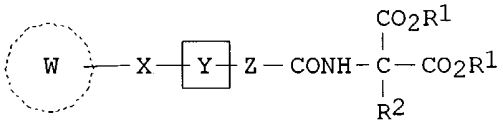

I

AB Described are malonic diesters derivs. represented by general formula [I; W = (un)substituted benzene, pyridine, quinoline, benzothiazole, pyrimidine, quinazoline, thienopyrimidine, or benzimidazole; X = NH, CONH; Y = (un)substituted benzene, naphthalene, pyridine, chroman, or 1,3-thiazole; Z = CH:CH, OCH2, OCMe2, NHCOCH2CH2, or (CH2)n; wherein n =

03; R1 = C1-4 lower alkyl; R2 = H, C1-4 lower alkyl or alkoxycarbonyl] and pharmacol. acceptable salts thereof being capable of preventing ICAM-1 and VCAM-1, which play the major roles among cell adhesion mols., from binding to leukocytes; and cell adhesion inhibitors containing as the active ingredient at least one of the above compds. and serving as excellent immunosuppressants, anti-inflammatory agents, antiallergic agents and tumor metastasis inhibitors. Thus, 2-[[4-(benzothiazol-2-ylamino)benzoyl]amino]acetic acid di-Et ester was condensed with aminomalonic acid di-Et ester using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride hydrochloride in the presence of 4-dimethylaminopyridine and Et3N in DMF at room temperature for 18 h to give 2-{2-[[4-(benzothiazol-2-ylamino)benzoyl]amino]acetamido}malonic acid di-Et ester. 2-[2-[4-(Benzothiazol-2-ylamino)-2-methoxyphenoxy]acetamido]malonic acid di-Et ester inhibited by 100% the binding of U937 cells to human umbilical vein endothelial cells (HUVEC) which was treated with human interleukin 1β to induce the expression of ICAM-1.

IC ICM C07C235-20
ICS C07C227-06; C07C229-24; C07C231-02; C07D213-38; C07D215-38; C07D235-30; C07D239-42; C07D239-47; C07D239-48; C07D239-94; C07D277-42; C07D277-44; C07D277-68; C07D277-82; C07D333-54; C07D417-12; A61K031-225; A61K031-38; A61K031-415

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST malonic diester prepn cell adhesion inhibitor 456312 564312; ICAM1 binding leukocyte inhibitor benzothiazole; pyridine contg malonic diester prepn immunosuppressant 651234; quinoline contg malonic diester prepn antiallergic 651234; benzothiazole contg malonic diester prepn antiinflammatory 651234; pyrimidine contg malonic diester prepn antitumor 651234; quinazoline contg malonic diester prepn antiinflammatory; thienopyrimidine contg malonic diester prepn immunosuppressant; benzimidazole contg malonic diester prepn antiallergic

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); preparation of malonic diester derivs. as cell adhesion inhibitors)

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(VCAM-1, binding of VCAM-1 to leukocytes, inhibitors; preparation of malonic diester derivs. as cell adhesion inhibitors)

IT Leukocyte
(binding of VCAM-1 to leukocytes, inhibitors; preparation of malonic diester derivs. as cell adhesion inhibitors)

IT Antitumor agents
(metastasis; preparation of malonic diester derivs. as cell adhesion inhibitors)

IT Allergy inhibitors
Anti-inflammatory agents
Cell adhesion
Immunosuppressants
(preparation of malonic diester derivs. as cell adhesion inhibitors)

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261348-39-4P 261348-40-7P 261348-41-8P 261348-42-9P 261348-43-0P
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261348-94-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malonic diester derivs. as cell adhesion inhibitors)

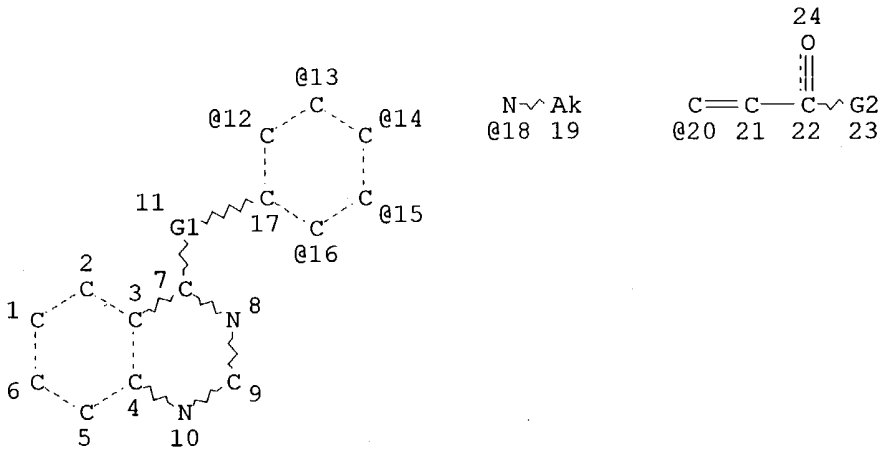
IT 74-88-4, Iodomethane, reactions 98-88-4, Benzoyl chloride 104-03-0, 2-(4-Nitrophenoxy)acetic acid 136-95-8, 2-Aminobenzothiazole 615-20-3, 2-Chlorobenzothiazole 638-07-3, Ethyl 4-chloroacetoacetate 1762-95-4, Ammonium thiocyanate 6279-86-3, Triethoxycarbonylmethane 13433-00-6 16017-69-9 17508-17-7, O-(2,4-Dinitrophenyl)hydroxylamine 20485-38-5 24257-59-8 102831-44-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of malonic diester derivs. as cell adhesion inhibitors)

IT 532-55-8P, Benzoyl isothiocyanate 4921-90-8P 6829-40-9P 14294-12-3P 261348-95-2P 261348-96-3P 261348-97-4P 261348-98-5P 261348-99-6P 261349-00-2P 261349-01-3P 261349-02-4P 261349-03-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of malonic diester derivs. as cell adhesion inhibitors)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'MARPATPREV' ENTERED AT 11:47:33 ON 09 NOV 2004

L21 STR



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DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 19
GGCAT IS LOC AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L24 0 SEA FILE=MARPATPREV SSS FUL L21 (MODIFIED ATTRIBUTES)

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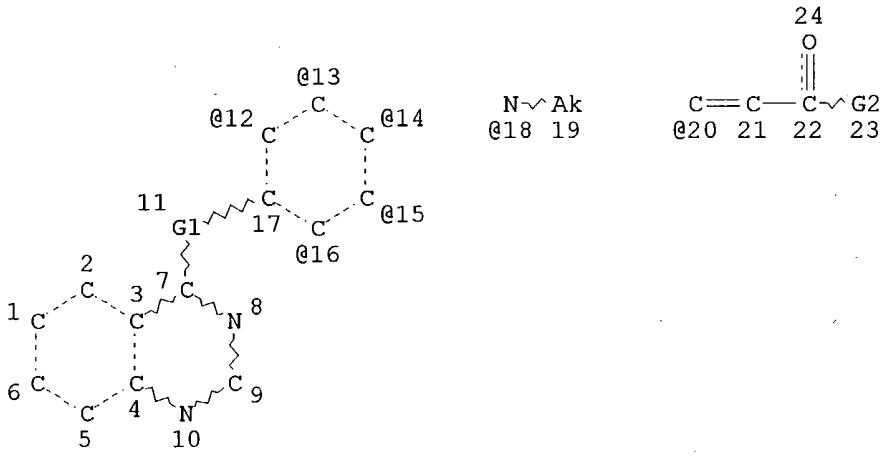
L21 STR



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DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 19
GGCAT IS LOC AT 19
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I

NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
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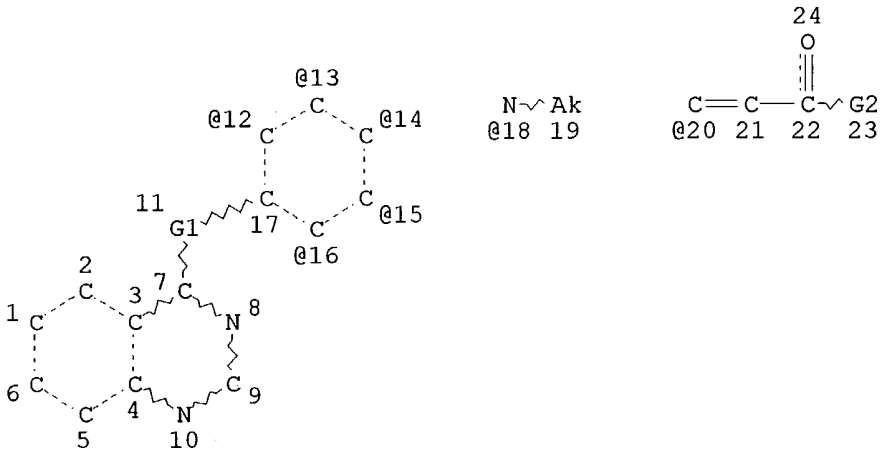

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VPA 20-12/13/14/15/16 U
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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
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FILE 'HOME' ENTERED AT 11:50:12 ON 09 NOV 2004